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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Roy A. Gravel et al.	Art Unit:	1633
Serial No.:	09/487,841	Examiner:	
Filed:	January 19, 2000		
Title:	HUMAN METHIONINE SYNTHASE REDUCTASE: CLONING, AND METHODS FOR EVALUATING RISK OF NEURAL TUBE DEFECTS, CARDIOVASCULAR DISEASE, CANCER, AND DOWN'S SYNDROME		

Assistant Commissioner of Patents
Washington, D.C. 20231

INFORMATION DISCLOSURE STATEMENT

Applicant submits the references listed on the attached form PTO 1449, copies of which are enclosed.

Submission of this statement is not a representation that a search has been made nor is information included in this statement an admission that the information is material to patentability.

Under 35 USC 120, this application relies on the earlier filing date of application serial number 09/371,347, filed on August 10, 1999. The following references were submitted to and/or cited by the Office in the prior application and, therefore, are not provided in this application:

Brasch et al., "Neonatal Megaloblastic Anemia Associated with Reduced Cellular Uptake of Folate and Low Methyl-B12 Levels: A New Mutation," Aust. N. Z. J. Med. 18 Supp.434 (1988).

Frosst et al., "A Candidate genetic Risk Factor for Vascular Disease: a Common Mutation in Methylenetetrahydrofolate Reductase," Nat. Genet. 10:111-113 (1995).

Goyette et al., "Human methylenetetrahydrofolate reductase: isolation of cDNA, mapping and mutation identification" Nature Genetics 7:195-200 (1994).

Gulati et al., "Defects in Auxiliary Redox Proteins Lead to Functional Methionine Synthase Deficiency," J. Biol. Chem. 272:19171-19175 (1997).

Hudson et al., "An STS-Based Map of the Human Genome," Science 270:1945-1954 (1995).

Leclerc et al., "Molecular Cloning, Expression and Physical Mapping of the Human Methionine Synthase Reductase Gene," Gene 12140:1-14 (1999).

Leclerc et al., "Cloning and mapping of a cDNA for methionine synthase reductase, a flavoprotein defective in patients with homocystinuria" *Proc. Natl. Acad. Sci. USA* 95:3059-3064 (1998).

Rosenblatt et al., "Altered Vitamin B_{12} Metabolism in Fibroblasts from a Patient with Megaloblastic Anemia and Homocystinuria Due to a New Defect in Methionine Biosynthesis," J. Clin. Invest. 74:2149-2156 (1984).

Rosenblatt et al., "Prenatal Vitamin B_{12} Therapy of a Fetus with Methylcobalamin Deficiency (Cobalamin E Disease)," Lancet 1:1127-1129 (1985).

Rozen, "Molecular Genetic Aspects of Hyperhomocysteinemia and its Relation to Folic Acid," Clin. Invest. Med. 19;171-178 (1996).

Schuh et al., "Homocystinuria and Megaloblastic Anemia Responsive to Vitamin B_{12} Therapy," N. Engl. J. Med. 310:686-690 (1984).

Tauro et al., "Dihydrofolate Reductase Deficiency Causing Megaloblastic Anemia in two Families," N. Engl. J. Med., case one 294:466 (1976).

van der Put et al., "Mutated Methylenetetrahydrofolate Reductase as a Risk Factor for Spina Bifida," The Lancet 346:1070-1071 (1995).

Watkins et al., "Functional Methionine Synthase Deficiency (cblE and CblG): Clinical and Biochemical Heterogeneity," Am. J. Med. Genet. 34:427-434 (1989).

Wilson et al., "A Common Variant in Methionine Synthase Reductase Combined with Low Cobalamin (Vitamin B_{12}) Increase Risk for Spina Bifida," Molecular Genetics and Metabolism 67:317-323 (1999).

This statement is being filed before the receipt of a first Office action on the merits. Please apply any charges or credits to Deposit Account 03-2095.

Respectfully submitted,

Date: May 18, 2000

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